

SEQUENCE LISTING

<110> Ikawa, Yoji
Otsuka Pharmaceutical Co. Ltd.

<120> Human p53 gene and its product

<130> P99-16

<140>

<141>

<150> JP P1998-100467

<151> 19 98-03-27

<160> 2.3

<170> PatentIn Ver. 2.0

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<211> 448

<212> PRT

<213> Human

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<221> DOMAIN

<222> (1).. (59)

<223> transactivation domain

<220>

<221> DNA BIND

<222> (142).. (321)

<223> DNA binding domain

<220>

<221> DOMAIN

<222> (353).. (397)

<223> oligomerization domain

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Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
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Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
50 55 60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
65 70 75 80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
85 90 95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
100 105 110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
115 120 125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
130 135 140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
145 150 155 160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
165 170 175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr

Sub A1

2/15

180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys
 405 410 415
 Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser
 420 425 430
 Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro
 435 440 445

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 <213> Human

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 <222> (145).. (1488)

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 <222> (2786).. (2791)

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 aaagaaagtt attaccgac cacc atg tcc cag agc aca cag aca aat gaa 171
 Met Ser Gln Ser Thr Gln Thr Asn Glu

mb
 81
 wv

180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys
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 420 425 430
 Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro
 435 440 445

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 <212> DNA
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 <222> (145).. (1488)

<220>
 <221> polyA signal
 <222> (2786).. (2791)

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 acagtactgc cctgaccctt acatccagcg ttctgtagaa acccagctca ttctcttgg 120
 aaagaaggtt attaccgata cacc atg tcc cag agc aca cag aca aat gaa 171
 Met Ser Gln Ser Thr Gln Thr Asn Glu

cga cgc tgc ttt gag gcc cgg atc tgt gct tgc cca gga aga gac aag 1083
 Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg
 300 305 310
 aag cgc gat gaa gat agc atc aga aag cag caa gtt tgc gac agt aca 1131
 Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp Ser Thr
 315 320 325
 aag aac ggt gat ggt acg aag cgc cgg ttt cgt cag aac aca cat ggt 1179
 Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr His Gly
 330 335 340 345
 atc cag atg aca tcc atc aag aaa cga aga tcc cca gat gat gaa ctg 1227
 Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp Glu Leu
 350 355 360
 tta tac tta cca gtg agt ggc cgt gag act tat gaa atg ctg ttg aag 1275
 Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu Leu Lys
 365 370 375
 atc aaa gag tcc ctg gaa ctg atg cag tac ctt cct cag cac aca att 1323
 Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His Thr Ile
 380 385 390
 gaa acg tac agt caa cag caa cag cag cag cag cag cag tta ctt cag 1371
 Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu Leu Gln
 395 400 405
 aaa cat ctg ctt tca gcc tgc ttc agt aat gag ctt gtg gag ccc cgg 1419
 Lys His Leu Leu Ser Ala Cys Phe Arg Asn Glu Leu Val Glu Pro Arg
 410 415 420 425
 aga gaa act cca aaa caa tct gac gtc ttc ttt aga cat tcc aag ccc 1467
 Arg Glu Thr Pro Lys Gln Ser Asp Val Phe Phe Arg His Ser Lys Pro
 430 435 440
 cca aac cga tca gtg tac cca tagagcccta tctctatatt ttaagtgtgt 1518
 Pro Asn Arg Ser Val Tyr Pro 445
 gtgtgtatt tccatgtgta taigtgagt taigtgtgt taigtgtgt cgtgtgtatc 1578
 tagccctcat aacaggact tgaagacat ttgtctaga gacccaactg ctcaaggcca 1638
 cnaagccact agtgagaga tctttgaag gactcaaac ctttacaaga aaggtgttt 1698
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 tggtcataag taagtgtag gtgactgaga gactcagta gacctttta atgtgtgtca 1998
 tgtaataata ttgcaagtag taagaacga aggtgtcaag tgaactgtt ggcagcgagg 2058
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 ccaactgtg ttggcatctg ttatgctaaa gtttttctg tacatgaac cctggaagac 2238
 ctactacaa aaactgtt ttggcccc atagcaggtt aactatttt gtgctttta 2298
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 gctcaaaata gaattigaag cctctcaca aaatcgtga ttaatttgt taattagac 2418
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mb
 A1
 21

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actctggac tggaaattaa agattgaaag gtagactac tttcttttt ttactcaaa 2598
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Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
35 40 45
Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
50 55 60
Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
65 70 75 80
Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
85 90 95
Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
100 105 110
Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
115 120 125
Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
130 135 140
Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
145 150 155 160
Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
165 170 175
Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
180 185 190
Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
195 200 205
Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
210 215 220
Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
225 230 235 240
Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
245 250 255
Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
260 265 270
Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
275 280 285
Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
290 295 300

Handwritten signature

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Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
305 310 315 320
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
325 330 335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
340 345 350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
355 360 365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
370 375 380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
385 390 395 400
Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys
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<223> transactivation domain

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<222> (353)..(397)
<223> oligomerization domain

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Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
35 40 45
Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
50 55 60
Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
65 70 75 80
Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
85 90 95
Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
100 105 110
Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
115 120 125
Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln

Sub
A1

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130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Glu Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
 435 440 445
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Ser
 500 505 510
 Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr
 515 520 525

*One
 81
 m*

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Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp
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Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys
545 550 555 560
Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His
565 570 575
Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser
580 585 590
Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg
595 600 605
Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe
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Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly
625 630 635 640
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aaagaaagtt attaccgntc cacc atg tcc cag agc aca cag aca aat gaa 171
Met Ser Gln Ser Thr Gln Thr Asn Glu
1 5
ttc ctc agt cca gag gtt ttc cag cat atc tgg gat ttt ctg gaa cag 219
Phe Leu Ser Pro Glu Val Phe Gln His Ile Trp Asp Phe Leu Glu Gln
10 15 20 25
cct ata tgt tca gtt cag ccc att gac tgg aac ttt ggg gat gaa cca 267
Pro Ile Cys Ser Val Gln Pro Ile Asp Leu Asn Phe Val Asp Glu Pro
30 35 40
tca gaa gat ggt gcg aca aac sag att gag att agc atg gac tgt atc 315
Ser Glu Asp Gly Ala Thr Asn Lys Ile Glu Ile Ser Met Asp Cys Ile
45 50 55
cgc atg cag gac tgg gac ctg agt gac ccc atg tgg cca cag tac acc 363
Arg Met Gln Asp Ser Asp Leu Ser Asp Pro Met Trp Pro Gln Tyr Thr
60 65 70
aac ctg ggg ctc ctg aac agc atg gac cag cag att cag aac agc tcc 411
Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn Gly Ser
75 80 85
tcg tcc acc agt ccc tat aac aca gac cac gcg cag aac agc gtc acc 459
Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser Val Thr
90 95 100 105
gcg ccc tgg ccc tac gca cag ccc agc tcc acc ttc gat gct ctc tct 507
Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala Leu Ser
110 115 120
cca tca ccc gcc atc ccc tcc aac acc gac tac cca ggc ccg cac agt 555
Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His Ser
125 130 135

And
Ahl

[illegible]

Ans
A11

1 st	2 nd	3 rd	4 th	5 th	6 th	7 th	8 th	9 th	10 th	11 th	12 th	13 th	14 th	15 th	16 th	17 th	18 th	19 th	20 th	21 st	22 nd	23 rd	24 th	25 th	26 th	27 th	28 th	29 th	30 th	31 st
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

Ans. A1

12/15

Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
435 440 445
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
450 455 460
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
465 470 475 480
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
485 490 495
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Ser
500 505 510
Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr
515 520 525
Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp
530 535 540
Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys
545 550 555 560
Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His
565 570 575
Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser
580 585 590
Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg
595 600 605
Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe
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Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly
625 630 635 640
Glu

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<212> DNA
<218> Artificial Sequence

<220>
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primer

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27

<210> 8
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<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:p73-R1
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tgctgcacgt tctccacgt ggacgtacg

29

<210> 9
<211> 29
<212> DNA
<218> Artificial Sequence

<400> 9
tacgataact acgacgtgta cgtgaggg 29

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~~<211> 29~~
~~<212> DNA~~
~~<213> Artificial Sequence~~

<400> 10
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{210} 11
 {211} 30
 {212} DNA
 {213} Artificial Sequence

<400> 11
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$\langle 212 \rangle$	DNA
$\langle 213 \rangle$	Artificial Sequence

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<210> 13
 <211> 20
 <212> DNA
 <213> Artificial Sequence

<400> 13
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<220>
 <223> Description of Artificial Sequence:p51-R2
 antisense primer

<400> 15
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19

<210> 16
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 <212> DNA
 <213> Artificial Sequence

<220>
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<210> 17
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 <212> DNA
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<220>
 <223> Description of Artificial Sequence:p51-R3
 antisense primer

<400> 17
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18

<210> 18
 <211> 19
 <212> DNA
 <213> Artificial Sequence

<220>
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 primer

<400> 18
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19

<210> 19
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:p51-R4
 antisense primer

<400> 19
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<210> 20
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 <223> Description of Artificial Sequence:p51-F5 sense
 primer

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<400> 20
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<212> DNA
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antisense primer

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<210> 22
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<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:p51-F6 sense
primer

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20

<210> 23
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<212> DNA
<213> Artificial Sequence

<220>
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antisense primer

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ctagtgccctt tgtgcctttg

20

and
A1
w